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Dermatopathology: An abridged compendium of words. A discussion of them and opinions about them. Part 5

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FASCICLES: a collection fusiform of oval or spindle-shaped cells, such as that which occurs in some "Spitz's nevi," in virtually all Reed's nevi, and in some melanomas. Also these may be found in the interweaving storiform pattern of Kaposi's sarcoma.

FENESTRATED: refers to a window-like pattern, the panes being formed of connective tissue (i.e., fibrous and sometimes mucinous), and the struts by cords and columns of epithelium. In cutaneous pathology; this pattern is observed most commonly in fibrofolliculoma and in fibroepithelial trichoblastic carcinoma.

FESTOONING: refers to the undulating pattern of the dermal papillae that are seen beneath subepidermal blisters of diseases like bullous pemphigoid and that resemble the folds of a curtain.

FETAL: designates a period intra-uterine development that begins when the product of conception reaches a crown-rump length of 30 mm, usually by 55 or 56 days after fertilization, and ends at the moment of birth. The product of conception during this period is called a fetus. The period before fetal is embryonic, and the product of conception during that earlier period is termed an embryo. Formation of tissues and development of their functions occur mostly during the fetal period.

FETUS: refers to the developing human or other animal, during the period in utero that extends from the end of the embryonic period, at the beginning of ninth week, to term. Many systems that began to develop in the embryonic period continue to advance during the fetal one. The rates of growth and gain in weight of a fetus are phenomenal. (SEE FETAL)

FIBER: a slender, elongated structure like that of a thread. By conventional microscopy, collagen is organized into bundles, whereas elastin is arranged in fibers. By electron microscopy, collagen is seen to be composed of fibers.

FIBRILLAR: manifesting a condition like fibrils, i.e., delicate slender stands of connective tissue, as do the collagen bundles in a neurofibroma.

FIBRIN: is a filamentous protein derived from fibrinogen by the action of thrombin during coagulation of the blood. It is seen in histologic sections stained by hematoxylin and eosin as fibrillary eosinophilic material.

FIBROCYTE: refers to a cell that produces fibers of fibrous and elastic tissue and ground substance of nonfibrous connective tissue. It is derived from mesenchyme and can differentiate toward other mesenchymal cells such as those that manufacture bone, cartilage, and muscle. In normal skin, a fibrocyte is characterized histologically by an oval nucleus and scant cytoplasm. Fibrocytes are responsible not only for synthesis of connective tissue proteins but for their repair and degradation. A single fibrocyte is able to synthesize, simultaneously, more than one type of collagen and elastin. Fibro-

cytes are important constituents of long-standing inflammatory conditions such as dermatofibromas, hamartomas such as fibrous papules, benign neoplasms such as infantile digital fibromas, and malignant neoplasms such as malignant fibrous histiocytomas. Strictly speaking, the term "fibroblast" refers to the stage of a mesenchymal cell when it is highly active and capable of dividing, in contrast to "fibrocyte," which denotes the same cell at a later stage when, although fully functional, it is incapable of dividing. For practical purposes, in the realms of cutaneous histology and pathology, the designation fibrocyte is preferable to fibroblast because it is in synchrony with other names for cells in normal skin and in tissues beneath it, such as keratocyte, melanocyte, histocyte, adipocyte, and chondrocyte.

No other cell in the skin is given the suffix blast (yet, at one stage, each of the types is dividing actively), and there is no compelling reason why cells that make fibers, i.e., fibrocytes, should be named differently from the others. Last, when viewed through a conventional microscope, it is not always possible on the basis of morphologic attributes to determine the stage of activity or the capability for division of the particular mesenchymal cell names "fibroblast" or "fibrocyte."

FIBROEPITHELIAL UNITS: are a combination of elements epithelial and fibrous that form a complex discrete, such combinations being separated from one another by clefts encircling, the pattern itself being indicative of benignancy. An example stereotypical of fibroepithelial units throughout a proliferation is found in trichofolliculoma, but also in trichoblastoma.

FIBROSIS: literally, means a condition of fibers and, figuratively, as it is used in surgical pathology, a condition of abnormal fibrous tissue that early in its sequence chronological tends to be accompanied by an increase in number of fibrocytes, those cells producing altered bundles of collagen and often an increase in the amount of ground substance. Later in its "life," fibrosis may take the form of sclerosis in which fibrocytes are decreased in number and collagen bundles no longer are discernible as discrete units, a condition termed misleadingly "homogenization of collagen."

Fibrosis is a consequence of any process pathologic that causes reduction in the amount of parenchyma and the framework of it, as occurs in acute inflammatory processes such as those that follow electrodessication and curettage, long-standing inflammatory processes such as caseous tuberculosis and gummatous syphilis and proliferations such as nodular trichoblastic (basal cell) carcinoma in which there may be extensive necrosis *en masse* of cells constituent. In general, the quantity of fibrosis is proportional to the extent of loss of tissue. Fibroplasia is a synonym for fibrosis. When fibroplasia occurs in response to a proliferation benign or malignant, the phenomenon is known as "desmoplasia."

As noted, fibrosis/fibroplasia may be present in the late stages of certain inflammatory skin diseases and also proliferative ones.

In addition, it may come into being in other pathologic processes such as the devolution of a verrucae vulgaris (a proliferation of epidermal keratocytes that fulfills the classic definition of "hyperplasia") located on a palm or sole, the residuum of that warty lesion being a kind of fibrotic papule; in a Clark's nevus (a "benign neoplasm" of abnormal melanocytes) in which "lamellar"/ "concentric" fibroplasia tends to develop immediately beneath the proliferation of melanocytes situated at the dermoepidermal junction of thin, elongated rete ridges; in certain examples of an intradermal Spitz's nevus (a benign neoplasm of abnormal melanocytes), they being marked by striking desmoplasia; in melanoma (a malignant neoplasm of abnormal melanocytes) that also may be characterized episodically by extensive desmoplasia, and in some carcinomas metastatic to skin in which desmoplasia may be rife.

FIBROUS SEPTA: are struts formed of bundles of collagen and fibrocytes that separate compartments, such as lobules of adipose tissue, from one another. In sections of normal subcutaneous tissue, fibrous septa are thin and outline rectangles of fat lobules.

FIBROUS TISSUE: refers to a type of connective tissue that consists of bundles of collagen manufactured by fibrocytes. Fibrocytes produce both the fibrillar and nonfibrillar components of fibrous tissue, such as mucosubstances.

FIBROUS TRACTS: linear bands of fibrous tissue that form normally behind hair follicles that have retracted in telogen.

FIGURATE: the term "figurate" refers to particular shapes of lesions clinically (those often being present together in the same patient at the same time), namely, arciform, annular, and polycyclic.

FIGURATE ERYTHEMAS: the diseases designated "so-called" figurate erythemas are not related to one another; the diseases so designated have in common only the presence, clinically of lesions with arcuate, annular, and polycyclic shape.

The "figurate erythemas" as usually conceived consist of erythema annulare centrifugum (Darier)-deep type, deep gyrate erythema, deep figurate erythema, palpable migratory and arciform erythema, erythema figuratum, erythema perstans, erythema annulare centrifugum, and many others. These are nothing more than patterns that may be formed by infiltrates of various condition, all of which may sometimes present clinically with annular, arcuate, gyrate, or figurate lesions

and at other times not. Therefore figurate erythemas as such are not a distinctive clinicopathologic entity and the term need not be used. (It should be noted however that erythema annulare centrifugum is a distinctive disease, which is totally unrelated to the non-diagnostic designation erythema annulare centrifugum, deep type.)

In addition, the group should include other equally dissimilar conditions such as subacute cutaneous lupus erythematous, erythema a marginatum, the urticarial stage of bullous pemphigoid, some plaques of mycosis fungoides, and one expression of psoriasis, none of those being found as a rule in classifications of the figurate erythemas in standard textbooks; all of the "figurate erythemas" are different from one another histopathologically because they are different from one another fundamentally and, that being the case, the notion of a category of "figurate erythemas" is as unuseful as that of "papulosquamous disease." (That is, not very useful.)

Further more, in any patient who presents with annular or figurate macules, papules, or plaques that show superficial and deep lymphocytic infiltrates, additional examinations and investigations need to be performed in order to diagnosis lupus tumidus, erythema migrans of borreliosis, herpetic infection, polymorphous light eruption, or even leukemia cutis, with specificity. They include clinicopathologic correlation, serology for antinuclear antibodies, PCR for herpes viruses and/or Borrelia on paraffin embedded biopsy specimens, and lymphocyte clonality investigations.

FISH: fluorescence in situ hybridization. Based upon genomic sites of interest identified via comparative genomic hybridization (CGH), commercially available probe sets have been developed that enable screening of paraffin-embedded tissue for chromosomal copy number changes that are closely associated with the diagnosis of melanoma.

FISSURE: a linear defect that extends from the surface of the skin into the dermis. Fissures tend to occur over flexural creases, especially of palms and soles affected severely by hyperkeratotic conditions such as psoriasis, pityriasis rubra pilaris, and chronic allergic contact dermatitis to ingredients of cement, as occurs in laborers such as hod carriers. The intergluteal cleft is another site favored for formation of a fissure in a lesion of psoriasis.

FLAME FIGURES: stellate shaped collections made up of granules of eosinophils that cluster around one or more bundles of collagen.

FLORET CELL: refers to a type of multinucleated giant cell in which fibrocytic or adipocytic hyperchromatic nuclei assume arrangements that resemble petals of a flower.

FOAM CELLS: are lipid-laden macrophages in which the pale cytoplasm contains numerous vacuoles from which lipids had been extracted during fixation in formalin and subsequent processing in alcohols of different grades. The lipid nature of the droplets can be demonstrated in frozen sections by fat stains such as scarlet red, oil red 0, or Sudan black. Foam cells are not specific for a single pathologic process, but predominate in lipidoses and xanthomatoses, a broad category of diseases characterized by deposits of excessive amounts of lipids in various organs of the body, including the skin. Any resolving inflammatory process associated with degradation of red blood cells consequent to extravasations of numerous erythrocytes, as well as inflammatory processes that involve adipose tissue with necrosis of adipocytes, i.e., lupus erythematosus profundus, may be accompanied by foam cells. (SEE CLEAR CELLS)

FOCAL ACANTHOLYTIC DYSKERATOSIS: a focus that consists of a suprabasal cleft above which there are acantholytic, dyskeratotic cells in the spinous and granular layers and, above them, a column of parakeratosis, some of the cells of which may have become acantholytic. This is a pattern and not a specific disease entity. There are several types. (SEE ACANTHOLYTIC DYSKERATOSIS)

FOLLICLE: means a very small sac of which there are many types in the body, i.e., hair follicles, thyroid follicles, lymphoid follicles, and ovarian follicles. In embryology and histology of the skin, and in the realms of cutaneous proliferations of all kinds, the word "follicle" pertains to "hair follicle" alone. The follicle of a hair includes matrical epithelium of the bulb that matures to become the hair itself, the inner sheath that envelops the hair, and the outer sheath that forms a sleeve around the inner sheath. In short, a follicle in anagen consists of two segments: a transitory lower segment of bulb and stem, and a permanent upper segment, the isthmus. The infundibulum is epidermal, not follicular. Every follicle, whether terminal or vellus, is surrounded by connective tissue, i.e., perifollicular sheath.

FOLLICULAR BULB: incorrectly termed hair bulb, refers to the pyriform lower end of a follicle whose boundaries are the base of the follicle below and the high-arched border known as Adamson's fringe above. That fringe also marks the lower boundary of the stem. The designation bulb derives from the morphologic similarity of a follicular bulb to a bulb of a tulip or an onion. A bulb consists mostly of matrical and supramatrical cells that mature to become cells of inner sheath and hair shaft. Signs of inner sheath differentiation are seen in the bulb in the form of trichohyalin granules and blue-gray corneocytes, and of impending hair in the form of a keratogenous zone. In addition to these constituents, strikingly dendritic melanocytes are disposed as solitary units in crescentic array at the base of a bulb above a follicular papilla. The melanin that they produce imparts color to hair.

FOLLICULAR GERM: imprecisely termed hair germ, is a primordium not only of a follicle, but of an entire follicular-sebaceous-apocrine unit. It is a crescentic collection of germinative cells whose nuclei are crowded and are situated at the base of an embryonic epidermis, below which are equally crowded nuclei of mesenchymal cells of an embryonic follicular papilla. The basal cells of a follicular germ are columnar and are aligned in a palisade. Follicular germinative cells consist mostly of nucleus, their cytoplasm being scant. Some nuclei are in mitosis.

FOLLICULITIS/PERIFOLLICULITIS: an inflammatory disease in which the infiltrate of inflammatory cells is present either in or around follicular epithelium, that is, epithelium of the isthmus, stem, and bulb. (SEE INFUNDIBULITIS/PERI-INFUNDIBULITIS)

FOLLICULO-SEBACEOUS-APOCRINE UNIT: refers to the entire structures that result from maturation and differentiation of a follicular germ in an embryo, to wit, a hair follicle in continuity with its adnexal sebaceous and apocrine units. As a follicular germ elongates and then differentiates, a hair follicle comes into being, and concurrent with it develop three bulges, the upper a putative apocrine gland and duct, the middle a future sebaceous gland and duct, and the lowest a place for attachment of smooth muscles of hair erection.

FOLLICULOTROPISM: adj. folliculotropic. a biological phenomenon that indicates growth or turning movement of a cell or a collection of cells toward a hair follicle. In a strictly morphologic sense, it is not definable since movement cannot be seen in the static tissues of a slide. The following terms would be better: intrafollicular—present within a hair follicle and perifollicular—present around a hair follicle.

Folliculotropism is not definable in medical dictionaries, or in textbooks of dermatopathology. However, it is constantly used in articles, especially in those about the histopathology of mycosis fungoides.

Folliculotropism and folliculotropic are employed, in general, for the mycosis fungoides in which "neoplastic" lymphocytes are mostly found in hair follicles. In fact, these criteria have led to two subtypes of mycosis fungoides, namely, the so-called folliculotropic and syringotropic.

There are only occasional exceptions in the usage in reference to entities other than mycosis fungoides, but interestingly nearly all are malignant: melanoma, bowenoid carcinoma, skin metastases of other carcinomas, etc. Descriptions of benign conditions with this term are extremely rare.

Apart from this term not being defined, there is no agreement among authors on its meaning. Despite the frequency with which folliculotropism is employed in mycosis fungoides, there is no agreement on whether lymphocytes should be in hair follicles only, if they could be intraepidermal too, or whether they should be accompanied by mucin in follicles. What dermatopathologists intend to describe by the word folliculotropic is those biopsies in which the lymphocytes are placed mostly in the epithelium of the hair follicle surface and infundibular, i.e., those specimens in which cells have a clear affinity for this adnexa, but this is not exclusive of mycosis fungoides.

Many other diseases, much more common and benign, display cells with tendency for adnexa. Any type of folliculitis, lupus erythematosus, lichen planopilaris, or Fox-Fordyce disease has a clear affinity for hair follicles, and neutrophilic hidradenitis or lichen striatus a tendency to affect sweat glands, to mention but some of them. The reason why none of these are described by words that finish with tropism or tropic is that dermatopathologists use these words only for malignant conditions. Confronted with exactly the same morphologic finding, namely, lymphocytes in hair follicles, folliculotropism is used only after having decided already on a malignant condition, usually mycosis fungoides. When the diagnosis of a benign condition, i.e., lupus erythematosus or neutrophilic hidradenitis, is made the cell infiltrates are not termed *tropic*. The term seems only to apply to lymphocytes, not to eosinophils or neutrophils. (SEE SYRINGOTROPIC)

FRINGE: describes the luminal border of a cell characterized by very fine filamentous projections. In a neoplasm, a fringe-like border of luminal cells indicates apocrine differentiation.

FUSIFORM: tapering toward each end, as is the situation with certain melanocytes that are constituents of "classic" Spitz's nevi. One type of melanocyte cytopathologic is a spindle truly, its shape being like that of a stick with ends tapered because of a thin oval nucleus and scant cytoplasm. Another type is fusiform, but rather than being thin, is distinguished by girth notable because of a plump oval nucleus and copious cytoplasm. In order to distinguish between those types of melanocytes in "classic" Spitz's nevi, we refer to the former as "spindle" and the latter as "fusiform," cognizant fully of the limitations of those designations. Parenthetically, nuclei of melanocytes of Reed's nevus are small and usually thin oval, and cytoplasm rich in melanin often is dendritic strikingly.

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GERM: is a term descriptive of a cluster of generative cells that in skin of an embryo gives rise to infundibular-apocrine-sebaceous-follicular units and to eccrine units. Those units derive from two different germs, both of which are situated at the base of surface ectoderm, the "follicular" germ being crescentic and apposed to a cluster of primitive mesenchymal cells of the future follicular papilla, and the eccrine germ

being shaped like a nubbin and devoid of any papilla of mesenchymal cells accompanying.

GERMINAL CENTERS: characteristic discrete round structures within lymphoid follicles, consisting of lymphocytes and macrophages that house nuclear debris of lymphocytes (tingible bodies). They occur as simulators of normal structures in inflammatory processes stimulating lymphomas and as abnormal structures in lymphomas such as giant follicular lymphoma (a malignant proliferation.)

GERMINATIVE CELLS: in a proliferation are analogues of those in a germ in an embryo that gives rise to the entire infundibular-apocrine-sebaceous-follicular unit, they being encountered in proliferations benign, i.e., trichoblastomas, and in ones malignant, i.e., trichoblastic (basal cell) carcinomas. "Follicular germinative cells" is the phrase employed as an abbreviation for cells germinative of the "future infundibular-apocrine-sebaceous-follicular unit."

GERM-LIKE: means resembling the germ in an embryo of the future infundibular-apocrine-sebaceous-follicular unit as occurs in trichoblastic (basal cell) carcinoma of types various, including superficial, nodular, fibroepitheliomatous, and infundibulocystic.

GERM AND PAPILLA: represent an association in an embryo of a germ at first crescentic but soon elongate and a papilla contiguous with it. That duo forms a unit responsible for giving rise to an entire future infundibular-apocrine-sebaceous-follicular unit. Simulations of the unit appear in proliferations various, ranging from trichoepithelioma to fibroepitheliomatous trichoblastic (basal cell) carcinoma, from fibrous papule of the face to nevus sebaceous, and from panfolliculoma to adamantinoid trichoblastoma.

GIANT MELANOCYTE: this term denotes not only cell size, but also implies that the cell contains several nuclei. Giant cells may be found in melanocytic nevi and in melanomas. Giant cells in melanocytic nevi are round and contain many small nuclei in the form of a rosette when clustered centrally. Less frequently the nuclei are arranged in a ring like configuration at the periphery.

GIANT MELANOSOME: a large, globular pigmented mass that may be seen with the conventional light microscope and is an abnormal melanosome many times larger than an ordinary melanosome.

GLAND: denotes a single epithelial cell or a group of cells, in a tissue or organ, specialized to elaborate and discharge substances that are used elsewhere in the body (secretion) or are eliminated from it (excretion). Glands that contain no excretory ducts, such as those of the adrenals and the thyroid, are referred to as endocrine glands, whereas those with excretory ducts, such as eccrine glands, apocrine glands, and sebaceous glands, are known as exocrine glands. The products of endocrine secretion enter blood or lymph directly, whereas those of exocrine secretion move directly onto body surfaces. The glands in skin are eccrine, apocrine, and sebaceous.

Eccrine glands are distributed over most of the body surface and promote cooling by evaporation of their secretion, i.e., sweat, which is produced by a method known as merocrine secretion. The long ducts of eccrine glands lead directly to the epidermis. Apocrine glands, vestiges of pheromone-secreting glands in lower animals, are situated in certain specific regions of the body, such as perianal and axillae. The long ducts of these glands connect to the mid portion of infundibular epidermis of follicles. The appearance of the distinctive secretion of apocrine glands as viewed by conventional microscopy has been likened to "decapitation" or "pinching off" because the tops of luminal cells appear to be severed from the remainder of them. "Decapitation" secretion and "pinching-off' secretion are synonyms for apocrine secretion. Sebaceous glands are found wherever there are follicles, mostly on the face, scalp, chest, and back. The glands consist of lobules composed of vacuolated cells and of ducts. The short ducts of sebaceous glands lead to the base of the infundibular epidermis. Sebaceous secretion is holocrine, which means that entire contents of sebaceous cell are discharged into a sebaceous duct.

GLASSY MEMBRANE: is a synonym for the PAS (periodic acid-Schiff) -positive basement membrane that surrounds the inferior segment of a hair follicle and is analogous to the basement membrane that separates epidermis from dermis. The follicular basement membrane thickens and becomes corrugated during the course of catagen.

GLOBULE: refers to a small spherical shape.

GLOBULES OF MELANIN: are small, spherical masses of melanin that are larger than the granules of melanin present in melanocytes and melanophages. Some term these "macroglobules" and others giant melanosomes. They are seen commonly in simple lentigines and in nevus spilus and uncommonly in a variety of other melanocytic lesions.

GLOMERULOID: means an appearance that resembles the glomerulus of a kidney, a structure that is formed by invagination of a capillary-rich mass of mesenchyme into a sac of epithelium. In the skin, some hemangiomas of POEMS syndrome are glomeruloid in foci.

GRADING OF MELANOMA: a scale of the degrees of "aggressiveness" in the biologic behavior of neoplasms based on cellular atypia or prevalence of mitotic figures. Many investigators have attempted to correlate the biologic activity of melanomas with the number of mitotic figures per unit area. The results they have reported are contradictory.

In practice, measurement of thickness of a melanoma with an ocular micrometer in the eyepiece of the microscope has proved to be the most reliable gauge of grade and therefore of prognosis.

The above was written by Maize and Ackerman in 1987. Now instead of grading, a staging system is used. It is the TNM system of the AJCC. However, it should be realized that prognostic "numbers" are only "statistics" and do not take into account the host that bears the "melanoma". Therefore assigning a prognosis to a patient based on a "number" in any field is a disservice to the patient.

GRANULATION TISSUE: highly vascular edematous connective tissue laced with a mixture of inflammatory cells. In skin, granulation tissue forms in response to trauma, such as incisions and puncture wounds, and below ulcers. Granulation tissue has been described clinically as "proud flesh," i.e., ulcerated, shiny, pink, sometimes moist tissue. The consummate example of granulation tissue in skin is seen in pyogenic granuloma at an early stage of it, that title being a misnomer because the condition is neither pyogenic nor a granuloma; it, fundamentally, is a proliferation of venules and capillaries secondary to trauma inflicted on a larger vessel, usually one situated in the deep reticular dermis or the upper part of the subcutaneous fat.

GRANULOMA: a collection of histiocytes, usually epithelioid ones. Epithelioid histiocytes (so termed because of their resemblance to epithelial cells, namely, oval nuclei, readily discernable eosinophilic cytoplasm, and some tendency to seeming cohesiveness) are predominant in granulomas of tuberculoid leprosy, whereas foamy histiocytes monopolize in granulomas of lepromatous leprosy; both epithelioid histiocytes and foamy histiocytes are present together in granulomas of dimorphous leprosy. Foamy histiocytes, known also as foam cells and lipophages, are nearly invariable in lobular panniculitides as a consequence of necrosis of adipocytes and are a finding, consistently, in xanthomas and xanthogranulomas. Multinucleate histiocytes, as well as mononuclear ones, may be found in a granuloma, and they have been given different names depending on nuances of them cytopathologically in regard especially to where nuclei are dispersed, for example, Langerhans, Touton, and foreign body, none of which has either specificity or is pathognomonic for any disease. A granuloma devoid of inflammatory cells other than epithelioid histiocytes is termed sarcoidal ("naked" tubercle), and that surrounded by a dense mantle of lymphocytes, and sometimes plasma cells, is designated tuberculoid. Sarcoidal granulomas are found not only in sarcoidosis, but also in foreign body responses to materials such as silica and beryllium. Tuberculoid granulomas are encountered in infectious diseases besides tuberculosis, among those being tuberculoid leprosy and the recidivans manifestation of leishmaniasis, and in noninfectious diseases such as rosacea and its variant, perioral/periocular dermatitis. Curiously, the granulomas of subcutaneous sarcoidosis tend to be tuberculoid in character and, episodically, granulomas of sarcoidosis restricted to the dermis may be tuberculoid. When epithelial histiocytes are aligned in the manner of stakes in a stockade, the arrangement is referred to as palisaded, as occurs in granuloma annulare, necrobiosis lipoidica, necrobiotic xanthogranuloma, and rheumatoid nodule. When histiocytes are dispersed between and among bundles of collagen, the pattern is designated interstitial, the exemplar of it being the interstitial manifestation of granuloma annulare. When an abscess is present in a collection of epithelioid histiocytes, as is common in infectious processes such as those initiated by atypical mycobacteria and deep fungi, the granuloma is known as suppurative. The term granuloma is employed clinically for smooth-surfaced, yellow-orange ("apple jelly") papules that house epithelioid histiocytes in tuberculoid pattern, as is seen in lupus vulgaris, or in sarcoidal pattern, as is observed in sarcoidosis, and for vegetations that represent suppurative granulomas of infectious cause, as is witnessed in chromomycosis and blastomycosis.

GRANULOMATOUS DERMATITIS: an infiltrate of inflammatory cells in which histiocytes predominate (in at least one high-power field). (SEE GRANULOMA)

GROUND SUBSTANCE: is the finely granular intercellular material of loose connective tissue in which cells and fibers are embedded. The ground substance is composed partly of glycoproteins and mucopolysaccharides, but mainly of nonsulfated hyaluronic acid. All of the cutaneous mucinoses are diseases of ground substance, i.e., focal mucinosis, pretibial myxedema, and myxedema

GUTTATE: drop-sized and-shaped. Usually applied to eruptive lesions of psoriasis (eruptive psoriasis may not be "guttate") and to one of the several manifestations of mycosis fungoides, i.e., the one ("guttate parapsoriasis") that is a variant of digitated dermatosis and is known also as small-plaque parapsoriasis, a flat manifestation of mycosis fungoides.

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HAIR: is a thread of compactly arranged corneocytes that represents the ultimate maturation of matrical cells situated at the base of a follicular bulb. Hair normally extends through an infundibular ostium and for various distances above the surface of the skin (i.e., far above the scalp of young persons and just above the margin of the eyelid). Hairs generally are of two types: terminal, which are relatively broad, long, and dark; and vellus, which are thin, short, and light.

HAIR DISC or HAARSCHEIBE: is a type of nerve ending purported to be positioned at the dermoepidermal junction by F. Pinkus in 1902. It is said to be a slow-adapting touch receptor present in mammalian skin. It is not visible, however, in sections of human skin stained by hematoxylin and eosin and viewed by conventional microscopy. No clear picture of this structure has ever been shown in any textbook of cutaneous histology, dermatology, general pathology, or dermatopathology.

HAMARTOMA: is a lesion identifiable by microscopy conventional as being characterized by an arrangement abnormal of tissues indigenous to a particular organ. The tissues in array aberrant appear to be normal at first glance, but may be abnormal slightly. The example stereotypical of hamartoma in the skin is nevus sebaceus, but conditions such as trichofolliculoma, fibrofolliculoma/ trichodiscoma, fibrous papule of the face, steatocystoma, and apocrine and eccrine nevi also are hamartomas. Because a hamartoma results from an error in development embryonic, the term "hamartoma" should not be applied to proliferations cellular that begin after tissues have reached maturity structural. For example, congenital melanocytic nevi of the deep type are hamartomas, whereas acquired melanocytic nevi such as those named eponymically for Spitz and Reed, are not, they being neoplasms benign. The distinction just made is supported by differences clinical, histopathologic, and biologic between melanocytic nevi that are present at or shortly after birth and those that become manifest long after birth. For practical purposes the term "proliferation" has been proposed to subsume the word hamartoma. (SEE PROLIFERATION)

HEMATOMA: a nodule that is formed by bleeding into the lower part of the dermis, subcutaneous fat, or both regions, usually as a consequence of trauma.

HENLE'S LAYER: is the outer component of the inner sheath of a follicle. In humans, it consists of only a single layer of cells, and it is the first layer of the inner sheath to display trichohyalin granules and to lose them in consequence of cornification. The layer is named for the early nineteenth century German histologist, T. Henle, who was the first to describe it.

HETERCHROMASIA: a difference in coloration in two or more structures or two or more parts of the same structure that under normal circumstances is alike in color, as is the case often in nuclei of a malignant neoplasm, such as melanoma, and at times in a benign neoplasm, such as "classic" Spitz's nevus.

HISTOCHEMICAL: denotes the study of particular tissues by analysis of their chemicals. Histochemical reactions result in colored products that indicate particular substances. For example, naphthol ASD-chloracetase esterases (Leder's stain) are used in cutaneous histopathology to localize esterases in granules of mast cells and in cells of myelogenous nature.

HISTOGENESIS: refers to evolution of tissue from inception to full development. The term is used commonly by general pathologists to denote origin of proliferations, when, in actuality, the origin of most proliferations is not known. For that reason, it is advisable to name the proliferations according to the composition of their cells and/or the differentiation of those cells. We, in the spirit of classic Virchowian pathology, advocate naming benign and malignant proliferations according to either; the specific type of cells of which they are composed of, and/or the specific differentiation of the cells themselves. Benign and malignant epithelial proliferations, for example, may be composed of keratocytes (i.e., seborrheic keratosis and squamous cell carcinoma), and benign and malignant nonepithelial proliferations may be made up of mast cells (i.e., urticaria pigmentosa and malignant mastocytosis). Benign and malignant epithelial proliferations may exhibit follicular, sebaceous, apocrine, and eccrine differentiation, and benign and malignant nonepithelial proliferations may show neural, muscular, vascular, fibrous, and adipose differentiation. Most epithelial and nonepithelial proliferations seem to represent faulty attempts at recapitulation of a homologous normal structure as it developed during the course of embryogenesis. All of these attempts fail, but some are more successful than others.

Those neoplasms that fail totally are considered to be undifferentiated, whereas those that succeed are deemed to be well-differentiated. By using repeatable and reliable criteria, specific, accurate diagnosis of benign and malignant epithelial and nonepithelial proliferations may be made histopathologically, except for those that are undifferentiated. There are exceptions. For example, some trichoblastomas, trichoblastic carcinomas of nodular type, and neuroendocrine carcinomas are undifferentiated, but each may be diagnosed with confidence at scanning magnification by virtue of particular characteristics.

HOLOCRINE: literally means, "separating entirely" and designates a gland or a secretion made by a gland in which the cells responsible for producing it rupture and release wholesale the materials (in the case mature sebocytes they being lipids) manufactured by them.

HOMOGENIZATION: of collagen refers to a uniform appearance of collagen as a consequence of seeming amalgamation of bundles with loss of the distinctive orthogonal pattern of them. The term is inaccurate because collagen cannot become homogenized. There can be sclerosis, as in late lesions of necrobiosis lipoidica, or packing of bundles of collagen, as in fully developed lesions of scleroderma, but not homogenization.

HONEYCOMB APPEARANCE: describes a pattern checkered made up of small aggregations of epithelial cells surrounded by mucin in abundance, that combination of elements forming units distinct separated from one another by thin fibrous septa, the overall architecture resembling a honey comb built by honeybees, the example quintessential of it in pathology cutaneous being mucinous carcinoma.

HORN PSEUDOCYSTS: whorls of delicate, laminated orthokeratotic cells that form in tunnels of infundibula, as within some seborrheic keratoses.

HUXLEY'S LAYER: is the middle component of an inner sheath of a follicle. It is two cells thick. Trichohyalin granules appear in Huxley's layer later than in Henle's layer, and they disappear from it later, too. That loss of trichohyalin granules occurs at Adamson's fringe and is accompanied by signs of cornification. The layer was discovered by zoologist, T.H. Huxley, in the mid-nineteenth century while he was still a medical student in London.

HYALINE: a substance that, when stained with hematoxylin and eosin and viewed by conventional microscopy, has a "glassy" homogeneous eosinophilic appearance. For almost a century; histopathologists used the term hyaline as a synonym for a substance considered by them to be specific and diagnostic of certain diseases, i.e., "toxic hyaline" for erythema clevatum diutinum. It is now appreciated that "toxic hyaline" is just fibrin. "Hyaline globules" is a name given to degenerating erythrocytes lodged in lysosomes of endothelial cells in some lesions of Kaposi's sarcoma. "Hyaline bodies" are necrotic keratocytes. The "hyaline" of hyalinasis cutis et mucosae (lipoid proteinosis) is largely hyaluronic acid. In short, the term hyaline is confusing because it does not convey specificity; and, for that reason, it should be avoided in favor of appellations for specific, definable substances, such as fibrin, erythrocytes, keratocytes, amyloid, and colloid.

HYALINE BODIES: necrotic keratocytes; also termed colloid bodies, Civatte bodies, and apoptotic bodies.

HYPERCHROMASIA (OVERCOLORATION): i.e., an increase in intensity of staining of nuclei as is seen often in a malignant neoplasm, such as melanoma. The three characteristics of nuclei said, conventionally, to be indicative of malignancy are large size, pleomorphism, and hyperchromasia. None of the three, however, is a sign unequivocal of malignancy. "Classic" Spitz's nevi, for example, often exhibit nuclei that are large and pleomorphic and, episodically, ones that are hyperchromatic. Surely a lymphoma cannot be distinguished from an inflammatory disease that simulates it, i.e., lymphocytoma cutis, by virtue of hyperchromasia of lymphocytes alone; whether lymphocytes are those of an inflammatory or neoplastic process, nuclei of them are so dark blue that they verge on black, which is as dark as they can get. A trio of changes more indicative of malignancy is crowding, pleomorphism, and heterochromasia dramatic of nuclei.

HYPERGRANULOSIS: increased thickness of the granular zone (stratum granulosum) of an epidermis, surface and/or infundibular, or of the upper part of an eccrine (or theoretically, an apocrine) duct as a consequence of an increased number of keratocytes whose cytoplasm contains keratohyaline granules either in loci or in continuity.

Hypergranulosis is a finding stereotypical for lichen planus, in which the granular zone tends to assume a wedge shape as a result of accentuation of keratohyaline-containing keratocytes in infundibula and acrosyringia. Hypergranulosis is a finding, consistently, in a variety of conditions as unlike as lichen simplex chronicus and bullous congenital ichthyosiform erythroderma. As a rule, hypergranulosis is coupled with a cornified layer marked by arrangement compactly of corneocytes. Two exceptions to that "rule" are (1) pityriasis rubra pilaris, in which hypergranulosis is associated with both orthokeratosis and parakeratosis, and (2) plane warts, in which hypergranulosis is covered by orthokeratosis arrayed in a basket-weave pattern.

HYPERKERATOSIS: a thickened cornified layer of an epithelium, usually an epidermis (surface and infundibular), but sometimes the upper part of an eccrine duct (and, theoretically, an apocrine duct). Hyperkeratosis may be classified as either orthokeratosis in which no nuclei are visible in cornified cells or parakeratosis, in which nuclei are retained overtly by cornified cells.

A more precise term for orthokeratosis is orthohyperkeratosis, the number of cornified cells actually being increased. The latter designation is awkward, however, and orthokeratosis being equivalent to parakeratosis in number of syllables and being the antonym of it, we invoke that term as license taken on behalf of simplification. Orthokeratosis may be subdivided into several types on the basis of pattern of arrangement of corneocytes, i.e., basket-weave, laminated (SEE LAMINATED ORTHOKERATOSIS), compact (SEE COMPACT ORTHOKERATOSIS), or a combination of them. Basket-weave orthokeratosis refers to a thickened cornified layer whose cells are arrayed in a criss-cross fashion that resembles the pattern in a woven basket, it is the same configuration, only thickened, assumed by the stratum corneum of normal skin anywhere on the integument except for palms and soles, where corneocytes are organized compactly. Two states pathologic in which the cornified layer may be thickened but still maintains its basket-weave character are the infections diseases tinea versicolor (caused by the fungus *Malassezia furfur* or *glabrosum*) and verrucae plana (caused by papillomavirus).

HYPERPLASIA: in classic pathology denotes a proliferation of cells that involutes when the stimulants for it ceases, such as occurs in verrucae vulgares. Unfortunately, the definition just set forth is not applicable to proliferations as they are assessed by microscopy conventional; as a rule, a histopathologist cannot identify in sections of tissue the stimulus responsible for a proliferation and moreover, in the majority of instances the stimulus is not known. Therefore, it is more useful to advise that the term hyperplasia characterize an increase in number of normal cells in arrangement relatively normal as is seen for example in so called syringofibroadenoma, i.e., a hyperplasia of epithelium of eccrine ducts that is induced by adjacent stroma altered markedly, such as fibrosis consequent to the effects of lymphedema long-standing, it being very different from apocrine fibroadenoma which is a benign proliferation of the type referred to conventionally as a neoplasm. In skin, most hyperplasias pseudocarcinomatous represent proliferation of epithelium of infundibular epidermis and of eccrine ducts. Because for purpose of diagnosis with specificity it matters not a whit whether a particular condition is termed neoplasm, hyperplasia, hamartoma, malformation, etc., the word "proliferation" as generic for all of them is used frequently in this work.

HYPOGRANULOSIS: a thinned granular zone as a consequence of a decreased number of cells containing keratohyaline granules. It may occur across the entire front of a lesion, such as in ichthyosis vulgaris or in foci of diseases as different as psoriasis, inflammatory linear verrucous epidermal nevus, and solar keratosis.